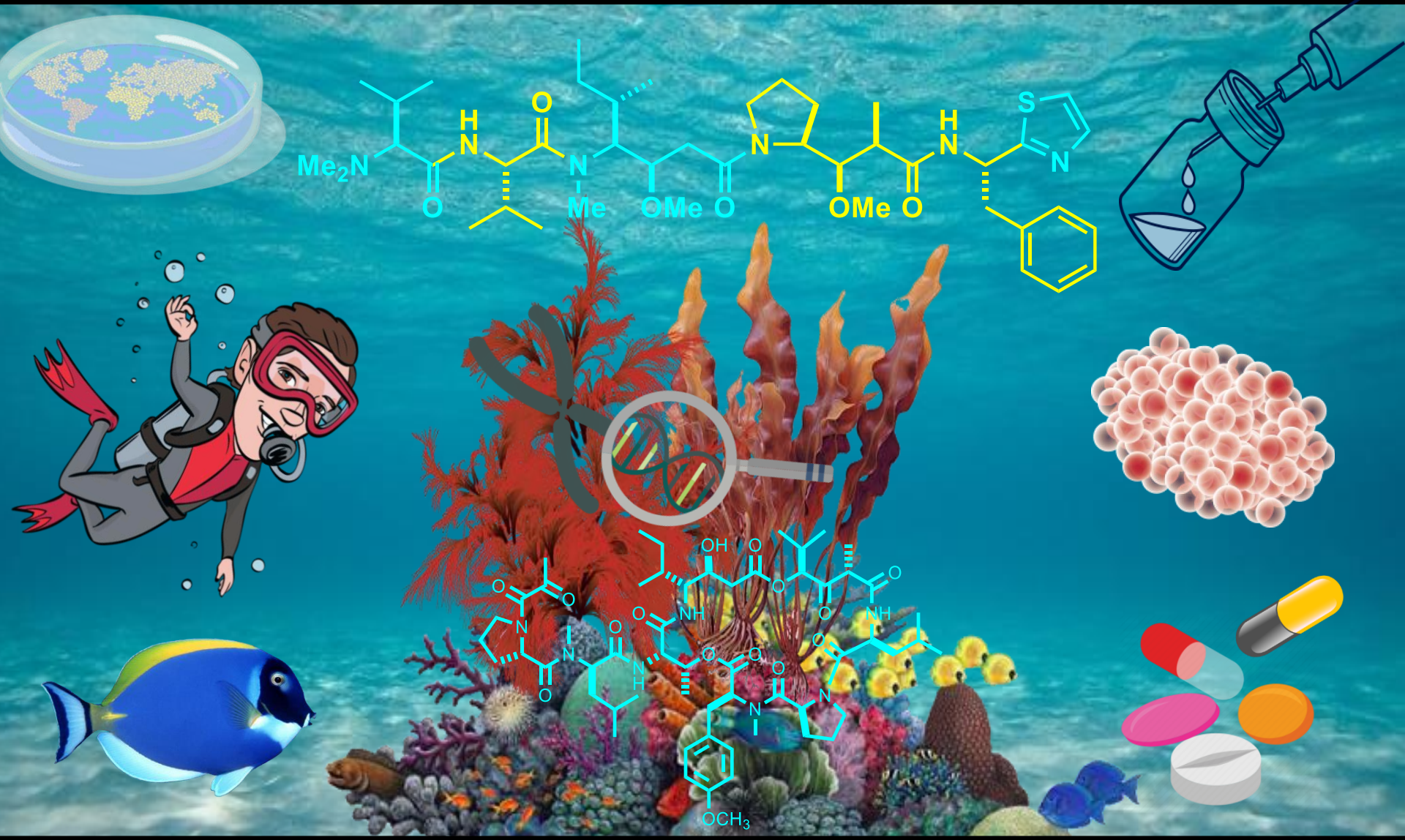
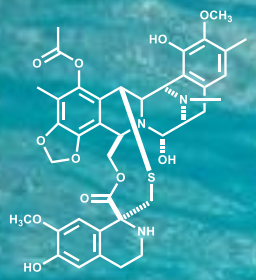
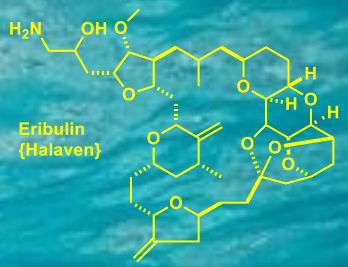
Marine Drugs



Dr. Omar M. Sabry

Marine Chemical Diversity



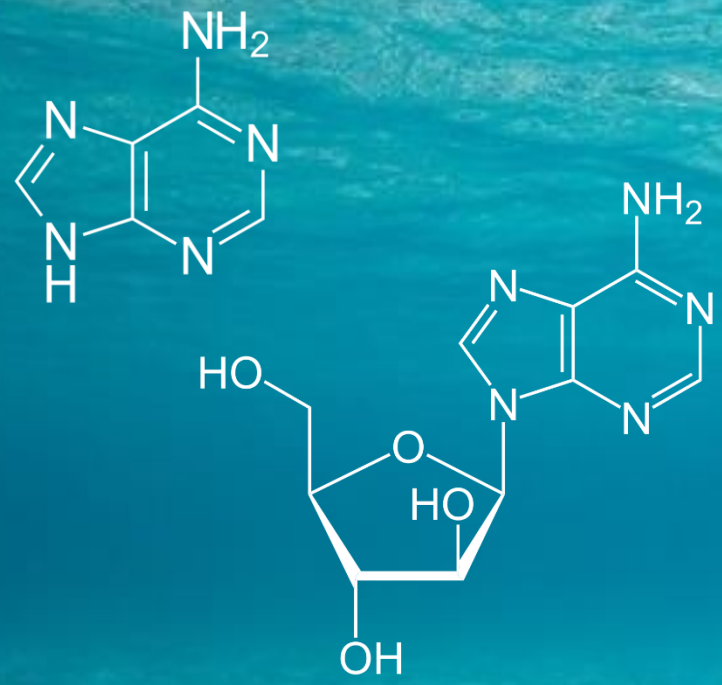


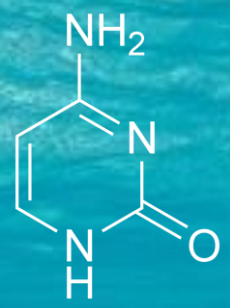
Chemical Diversity

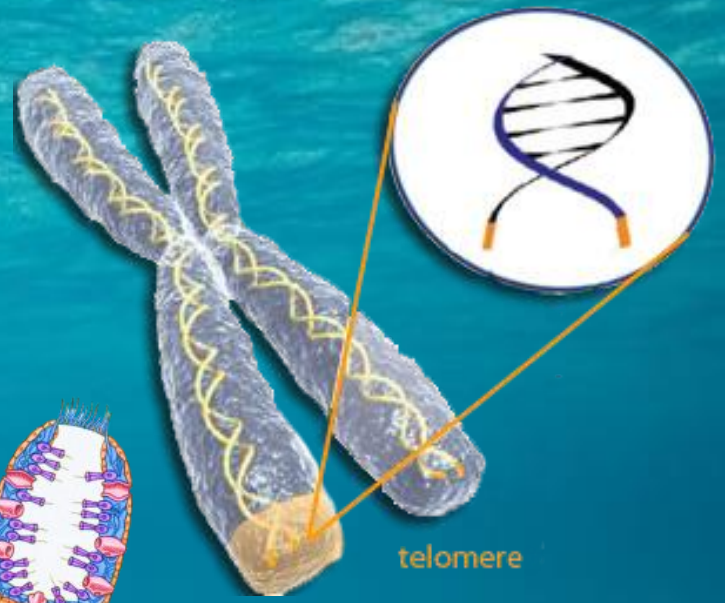
Nucleosides	Sponges	Blue Green Algae	**Linear Polypeptides**
Cyclic Polypeptides	Snails	Blue Green Algae	**Cyclic Depsipeptides**
Alkaloids	Tunicates	Sponges	**Polyketides**
Terpenoids	Corals	Fish	**PUFAs**

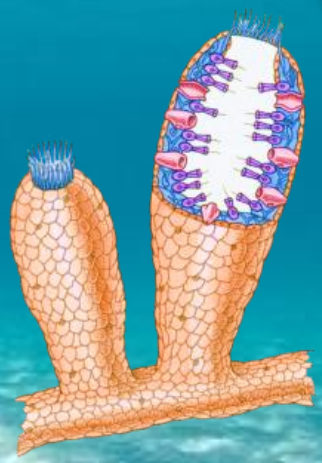
Nucleosides

- Adenine and Cytosine derivatives





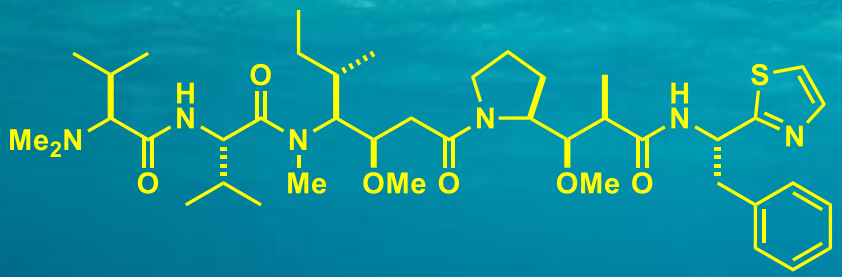




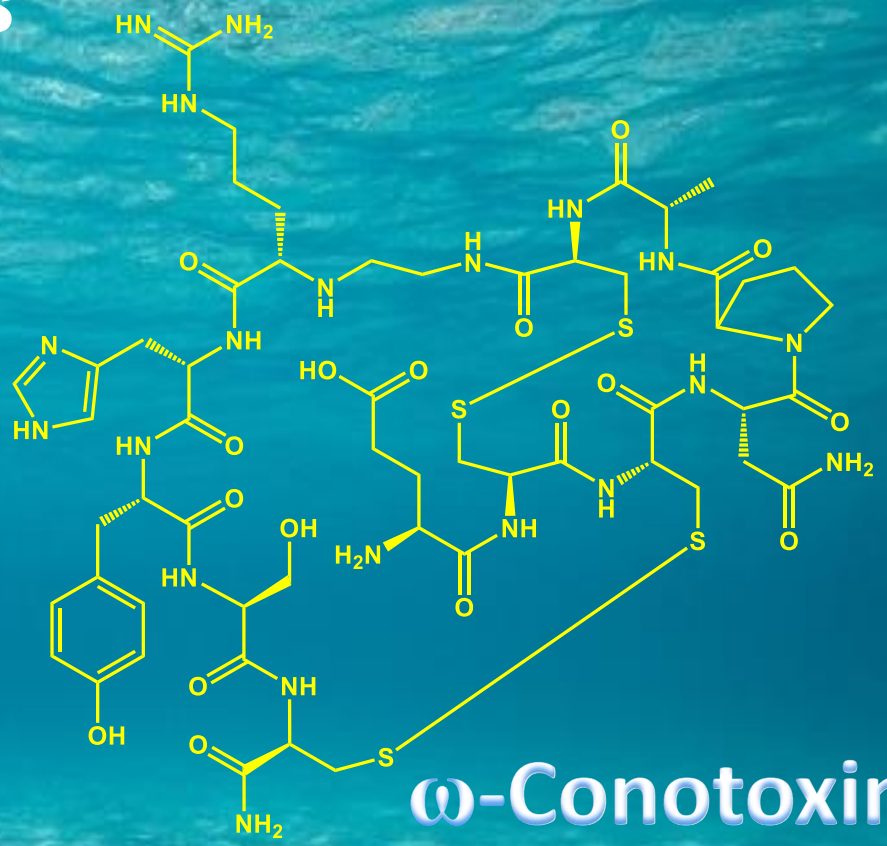
- Source: Sponge
- Uses: Antiviral and Anti-cancer

Polypeptides

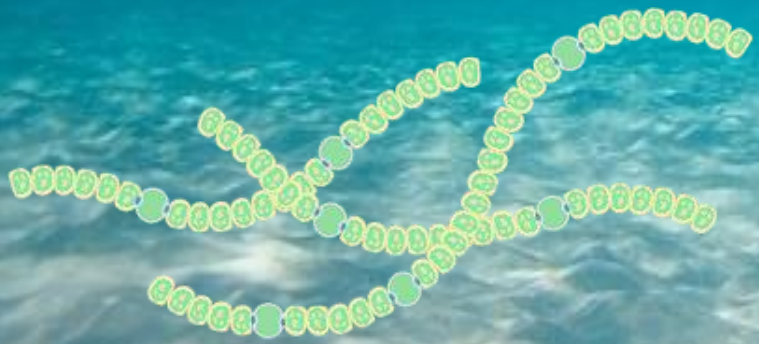
- Linear chain peptides
- Cyclic Peptides



Dolastatin 10

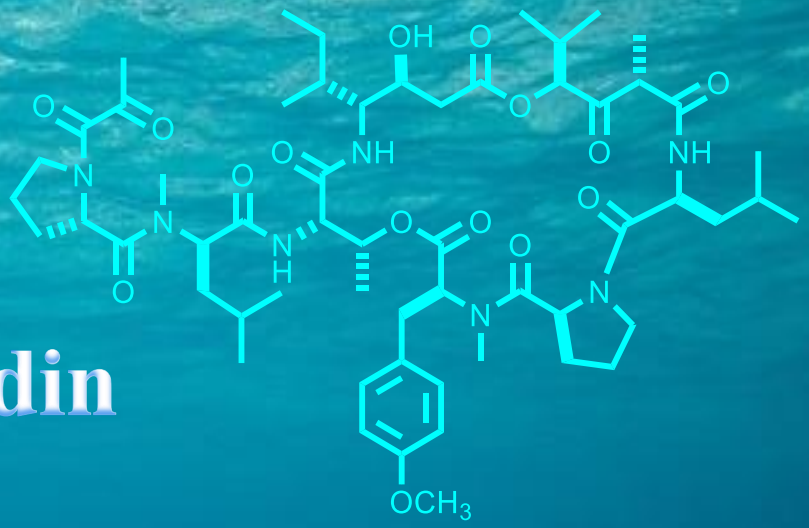


ω-Conotoxin



Polypeptides

- Linear chain depsipeptides
- Cyclic depsipeptides

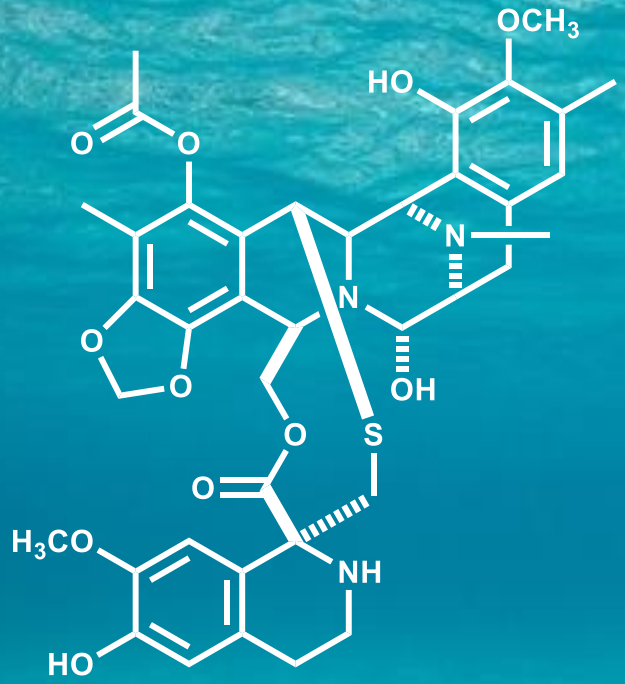


Aplidin

- Source: Cyanobacteria, nudibranchs, Tunicates and snails
- Use: Cancer

Alkaloids

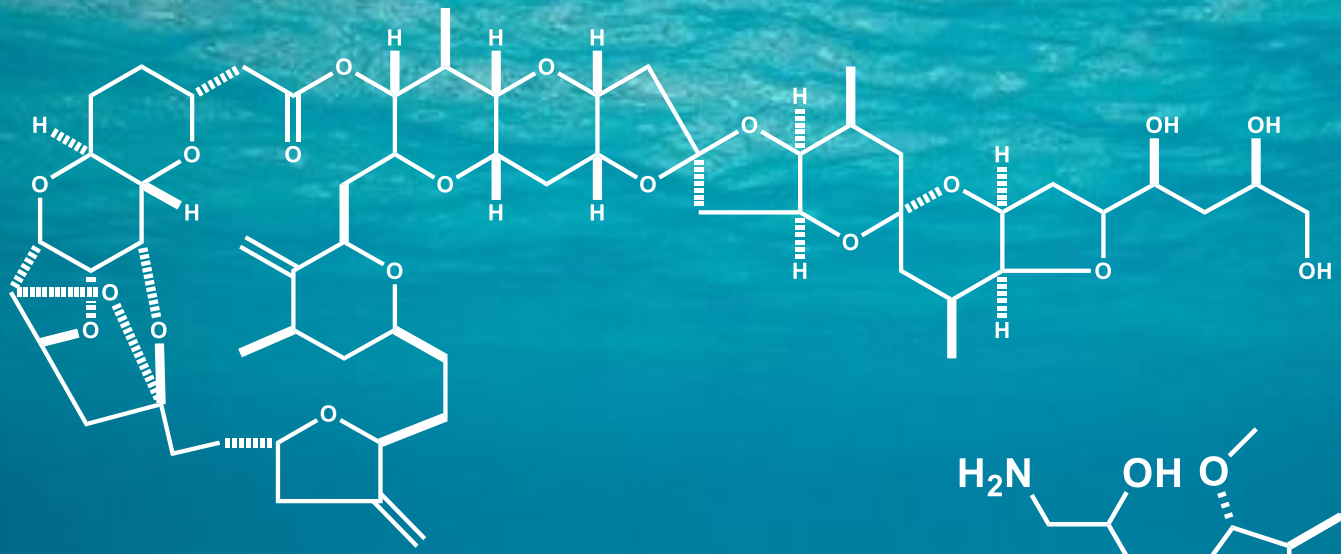
- Tetrahydroisoquinoline alkaloids



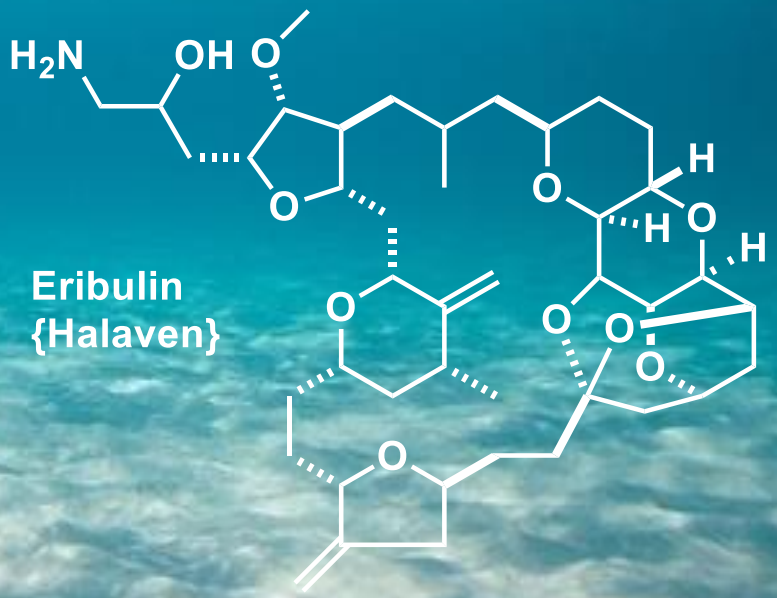
- Source: Tunicates
- Use: Anti-cancer {Alkylating agent}

Polyketides

- Halichondin B

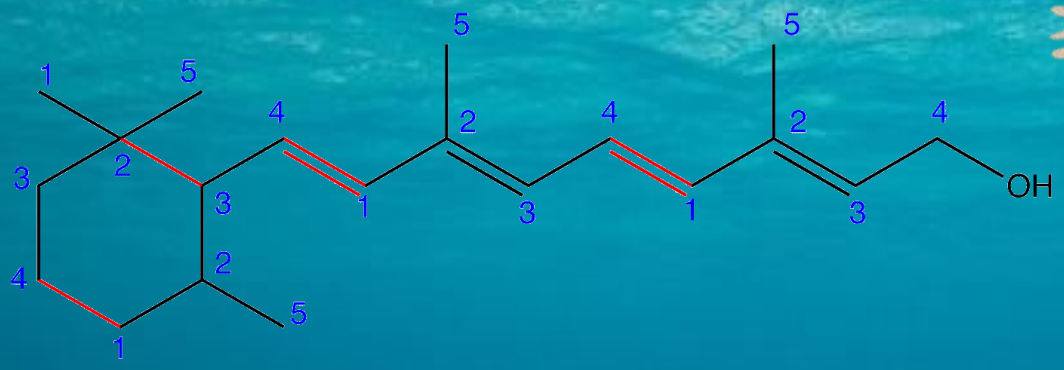


- Source: Sponge
- Use: Breast cancer



Eribulin
{Halaven}

Terpenoids

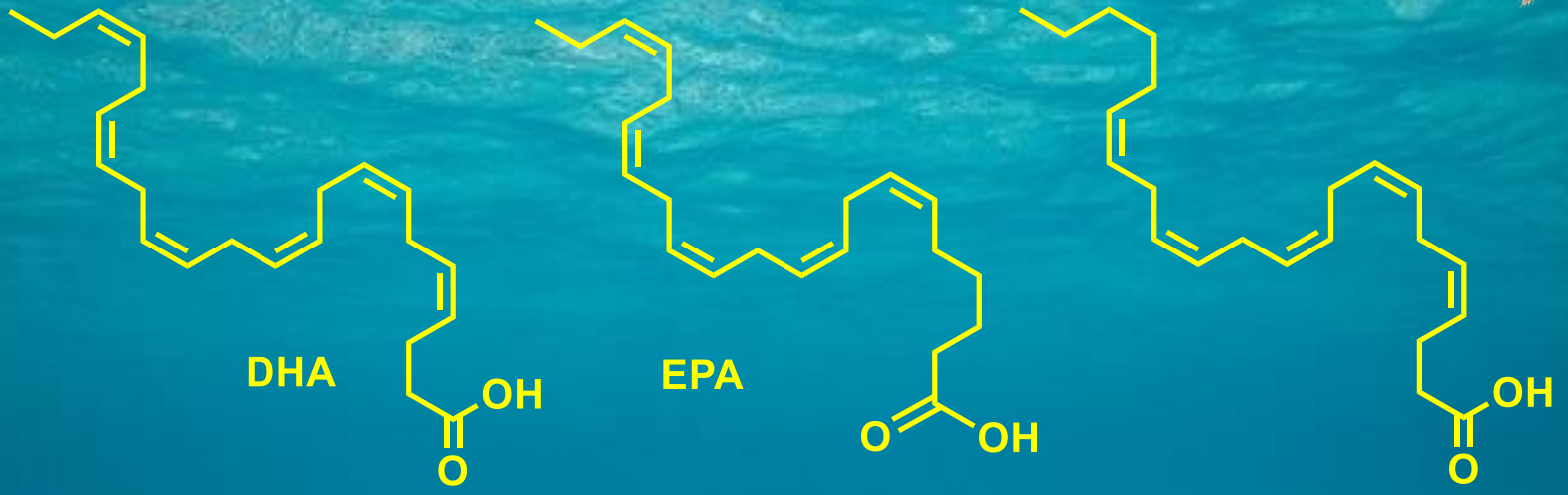


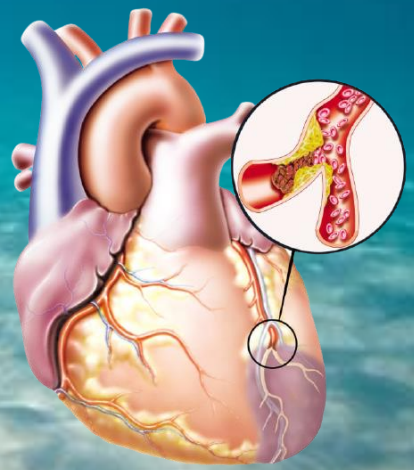
Source: Corals, Sponges and Brown algae}

Use: Inflammation

PUFAs {Lipids}

- Omega 3 {PUFA}



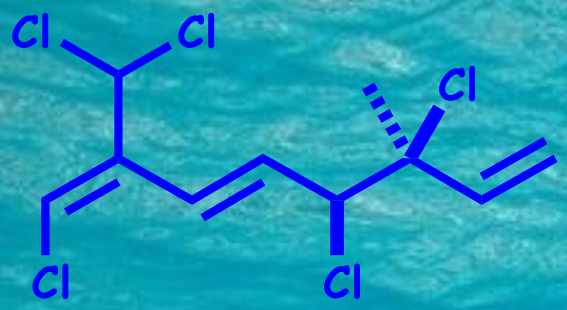


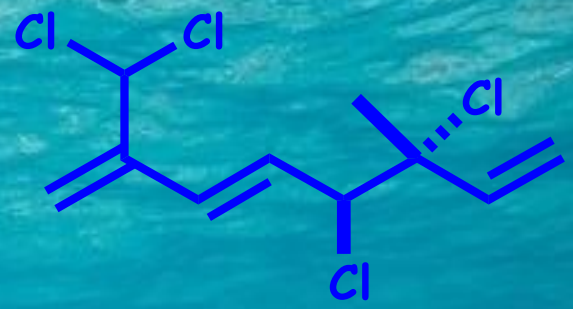
- Source: Fish
- Use: Cardioprotective

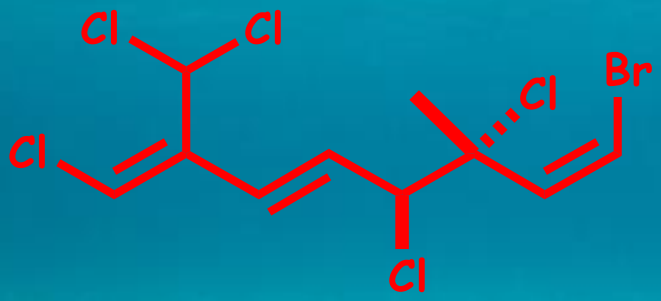
Sterols

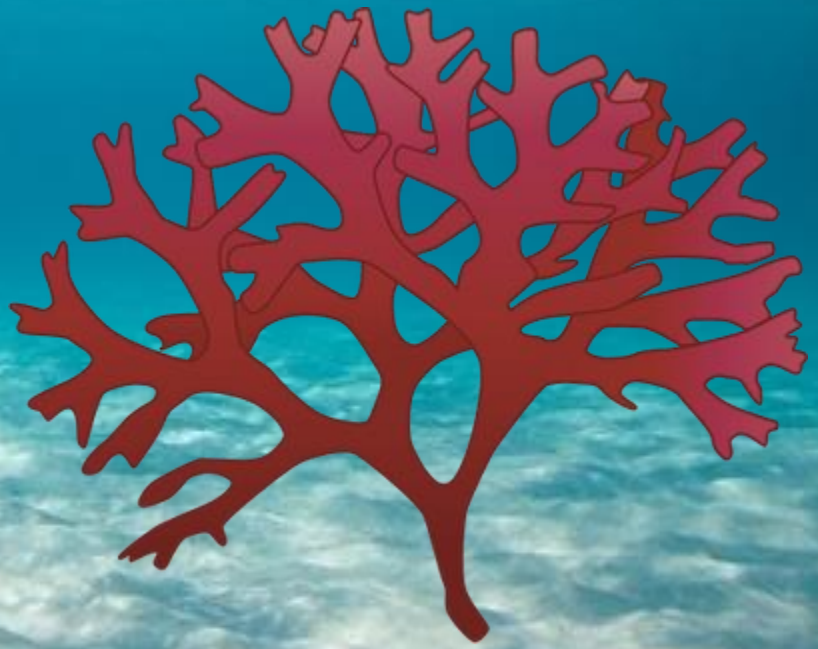
Source: Soft Corals - Green Algae

Polyhalogenated monoterpenes





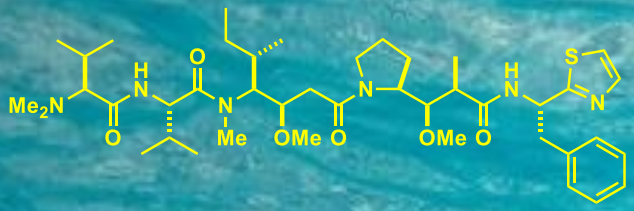




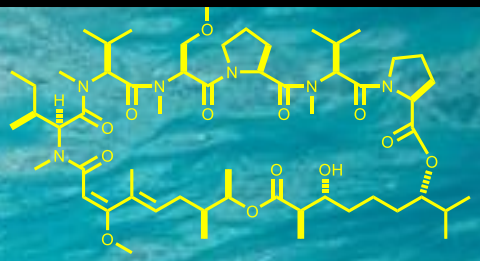
Source: Red algae

Use: Cytotoxic

Peptides: Drugs of Future

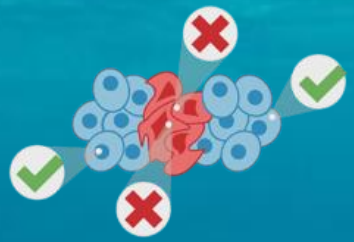


Peptides: Drugs of Future



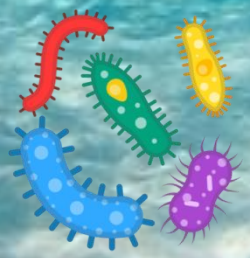
Selectivity

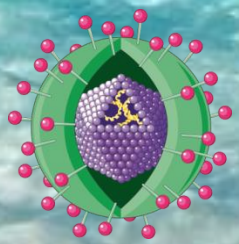
Low Concentration



Low Toxicity

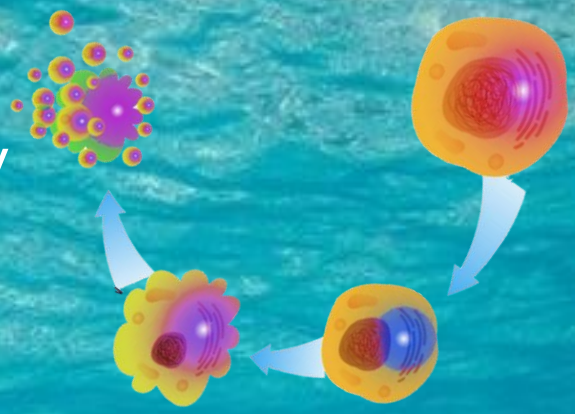
Diverse Biology





Bioactivities

- Anti-cancer activity
- Anti-inflammatory activity
- Anti-viral activity
- Cardio-protective activity

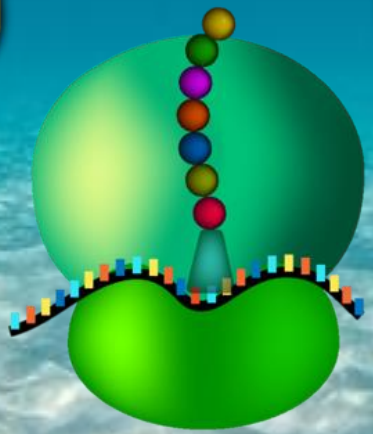


Peptides According to Biosynthesis

Polypeptides

Ribosomal Polypeptides RPPs

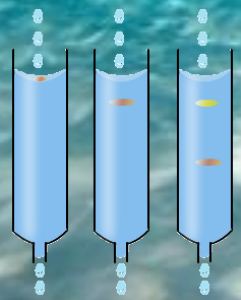
Non-Ribosomal Polypeptides NRPPs



Precautions of Polypeptides

Precautions of Polypeptides

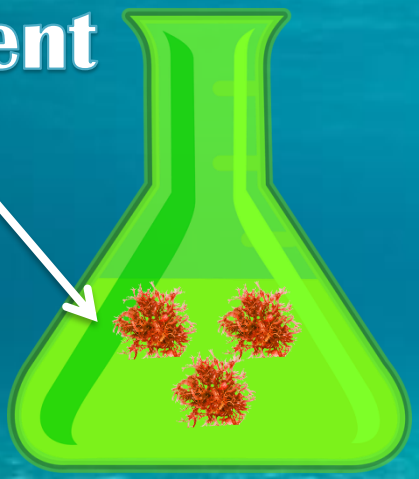
- During Extraction
- During Purification
- During Isolation
- During USE



Fractionation

Precautions During Extraction of Polypeptides

- Special precautions during extraction
- Extraction {Soon}



Sample Extraction

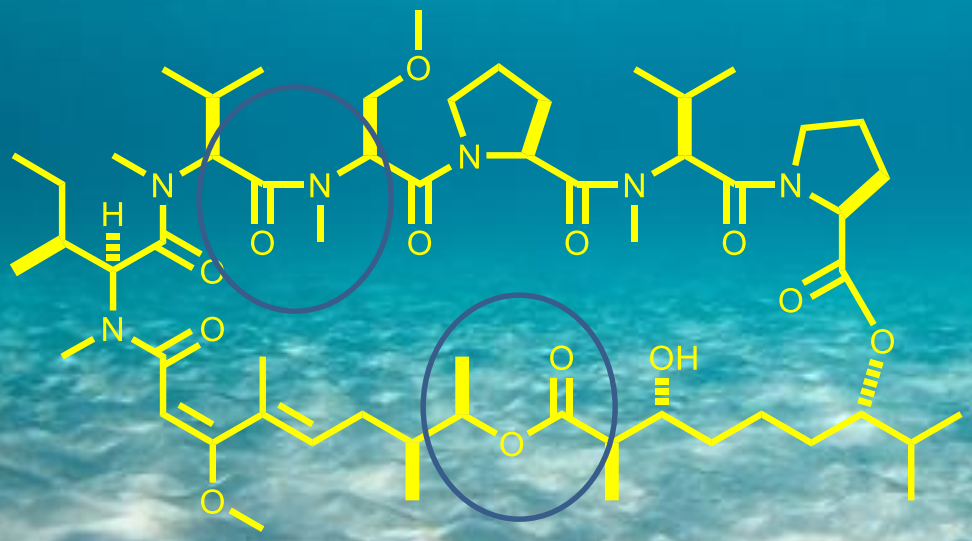
Solvent Evaporation

Fractionation

Depsipeptides

Depsipeptides

Definition

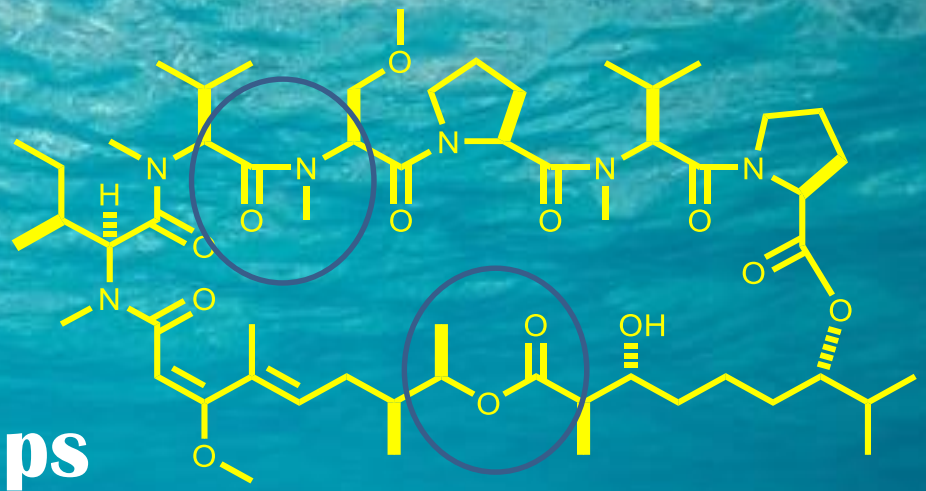


Identification

pepsin enzyme

IR

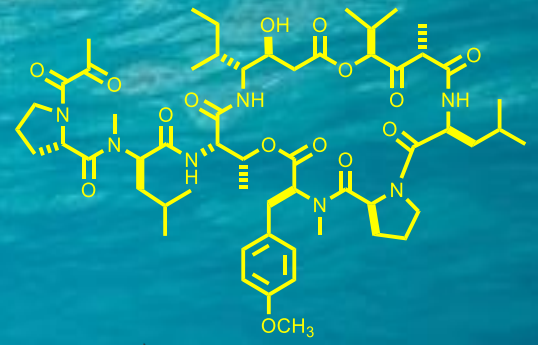
Depsipeptides

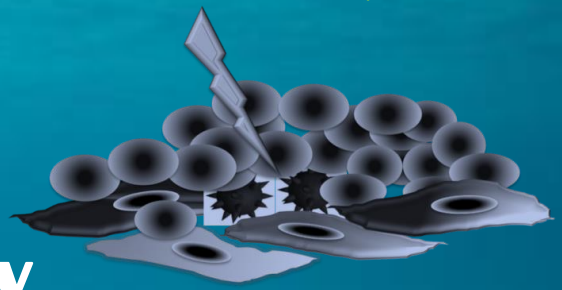


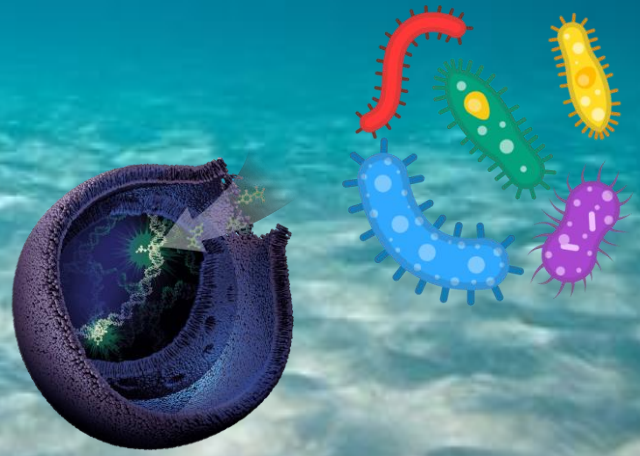
- Chain of amino acids
- Linked by amide groups
- Alternating with carboxylic acids
- Linked by ester group
- Source:
  - Cyanobacteria {Blue green algae}
  - Snails
  - Tunicates
  - Nudibranchs - Microbes

Depsipeptides

- Drugs of future
  - Highly specific mode of actions
  - Needed in lower doses
  - Have reduced risk of toxicity
  - Used for bacterial infections
  - Have anti-inflammatory activity
  - Inhibits HIV
  - Strong anti-cancer activity

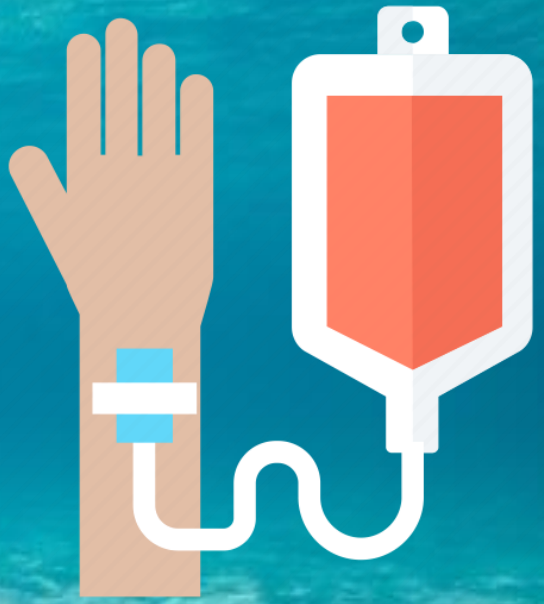






Depsipeptides

- Can’t be administered orally
- Intravenous route



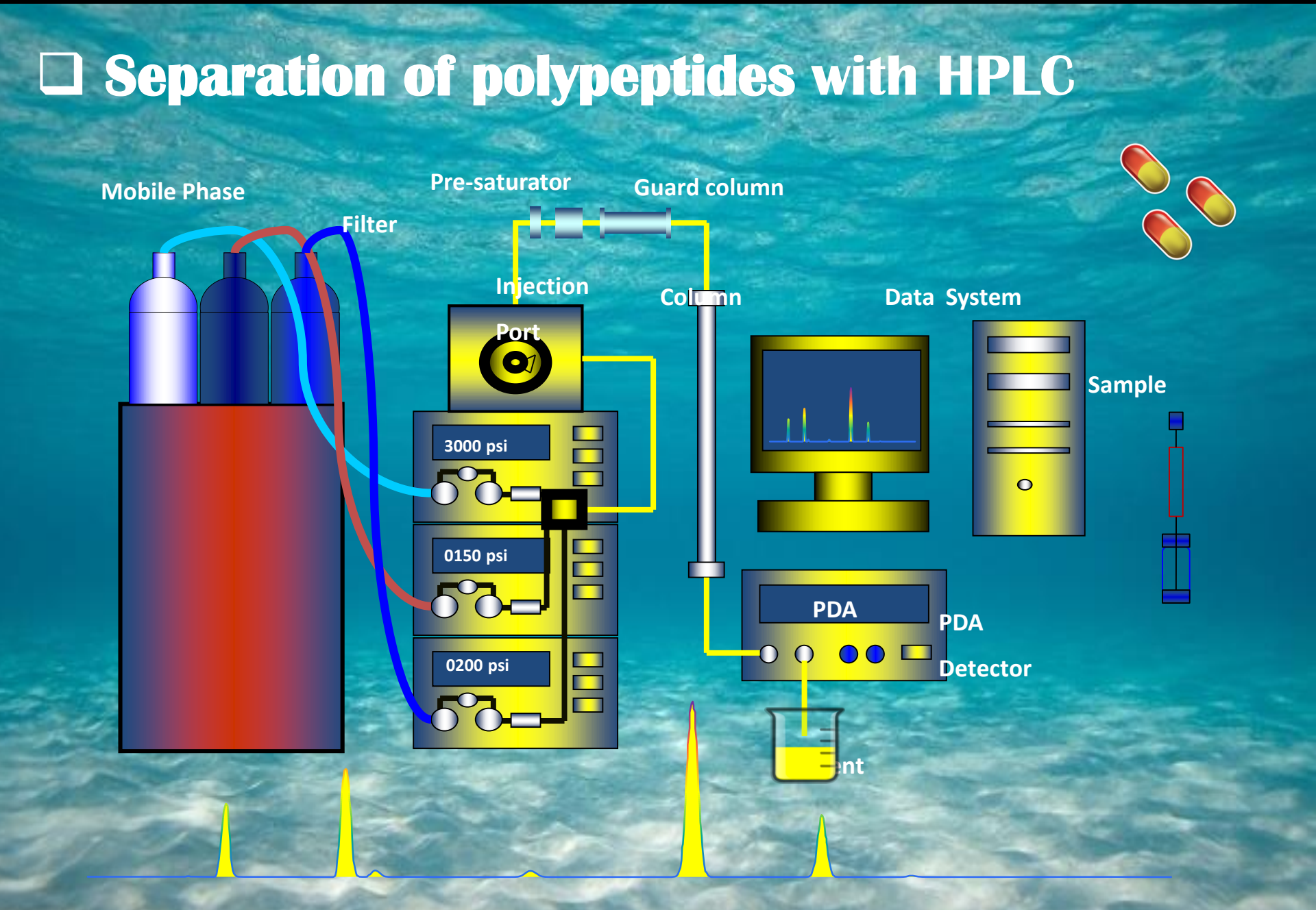
Depsipeptides

- Organic solvents for extraction process
  Not hydrophilic solvents.

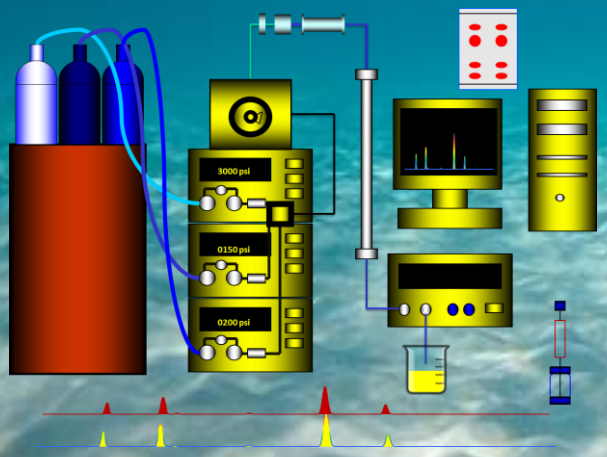
CH_2Cl_2/CH_3OH 3:2

Isolation of Marine Polypeptides

❑ Separation of polypeptides with HPLC



Single λ UV Detector



Mercury Lamp

Slit

Sample

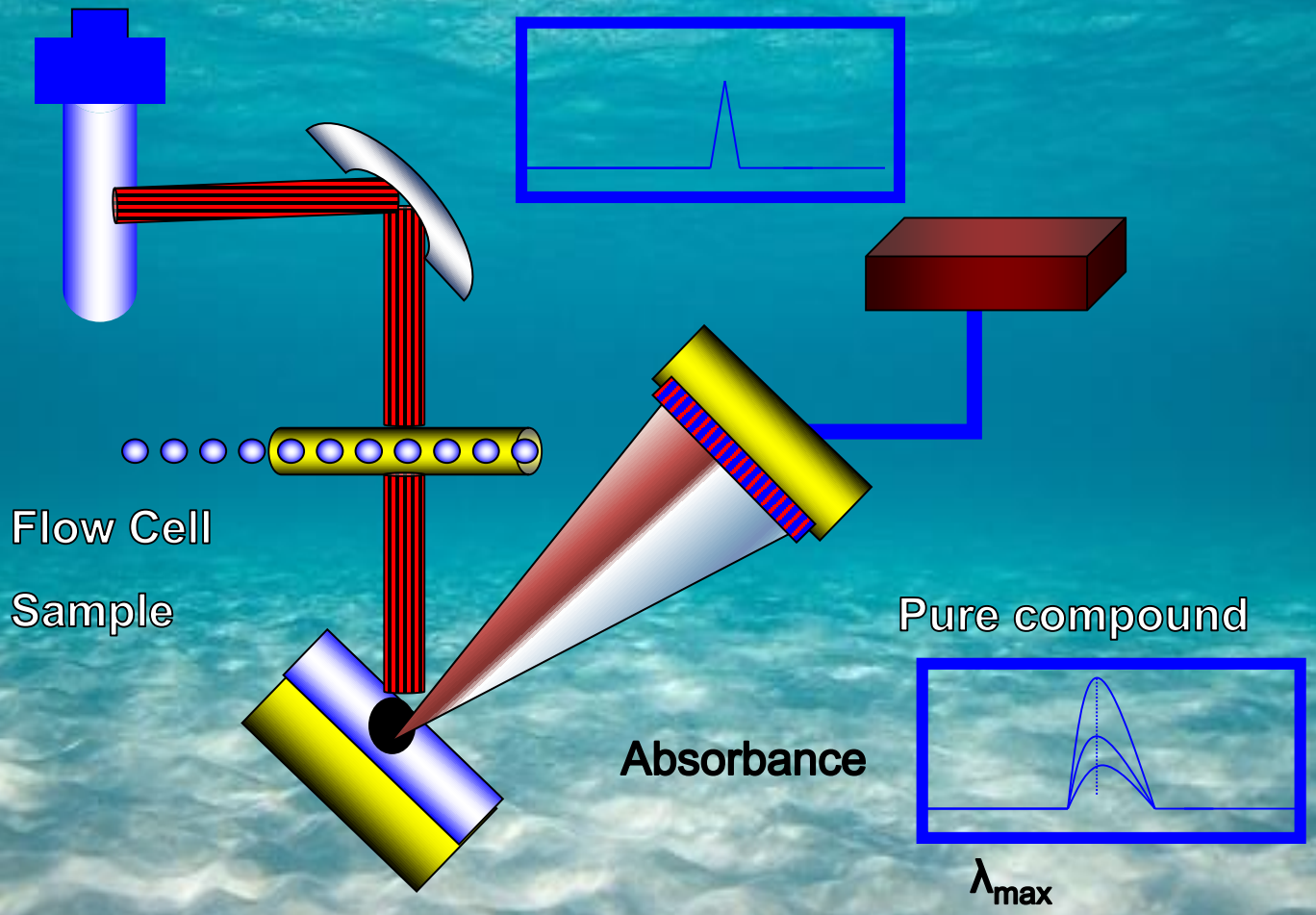
Chromatogram

Amplifier

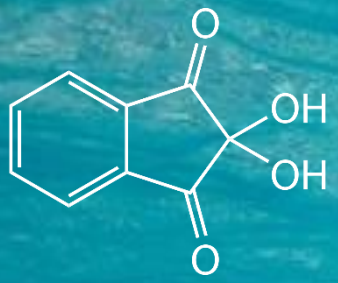
Diode Array

Polypeptides

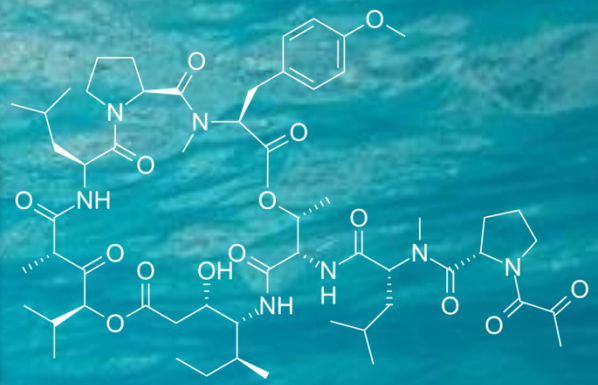
- PDAD {Photo-Diode Array Detector} during separation of cyclic depsipeptides with HPLC



Identification of Marine Polypeptides



Identification of Marine Polypeptides

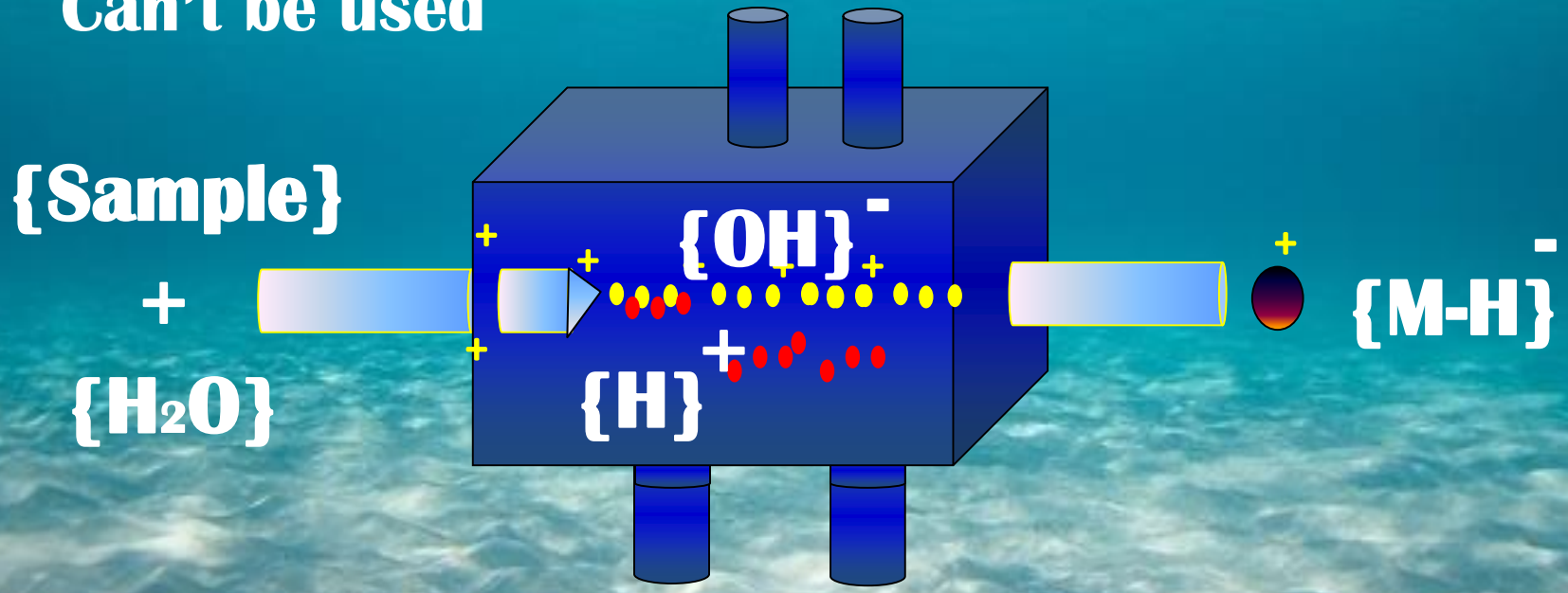


- Nin Hydrin
- MS
  Mass Spectroscopy
- 1HNMR

Polypeptides

- **ESIMS** {Electro Spray Ionization Mass Spectroscopy}
- **EIMS** {Electron Impact Mass Spectroscopy}

Can't be used

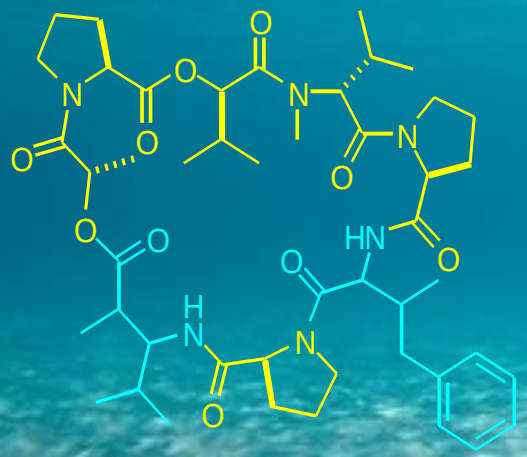


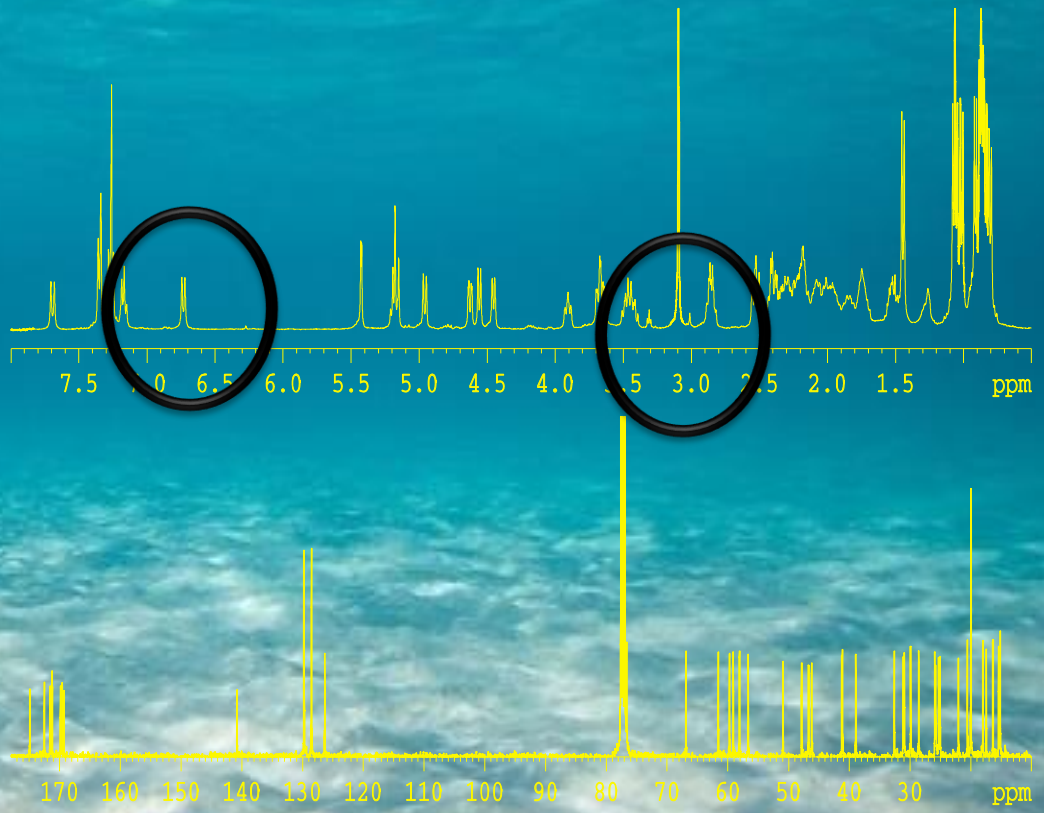
Polypeptides NMR

1HNMR signals

Amide (δ 6.40 - 6.95) ppm

N-methyl amide (δ 2.85 – 3.10) ppm

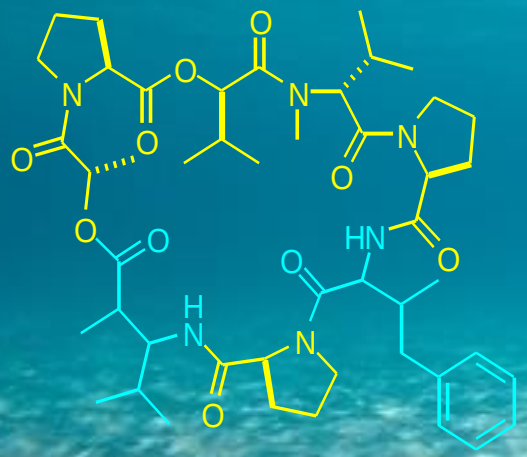


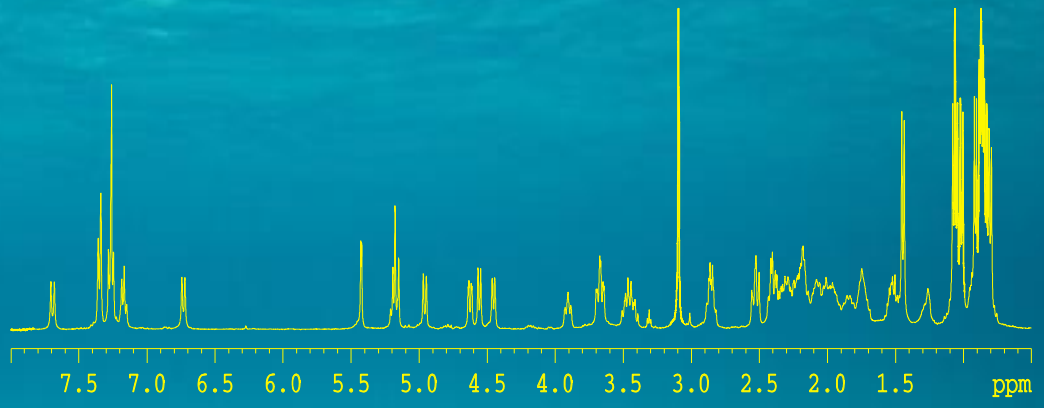


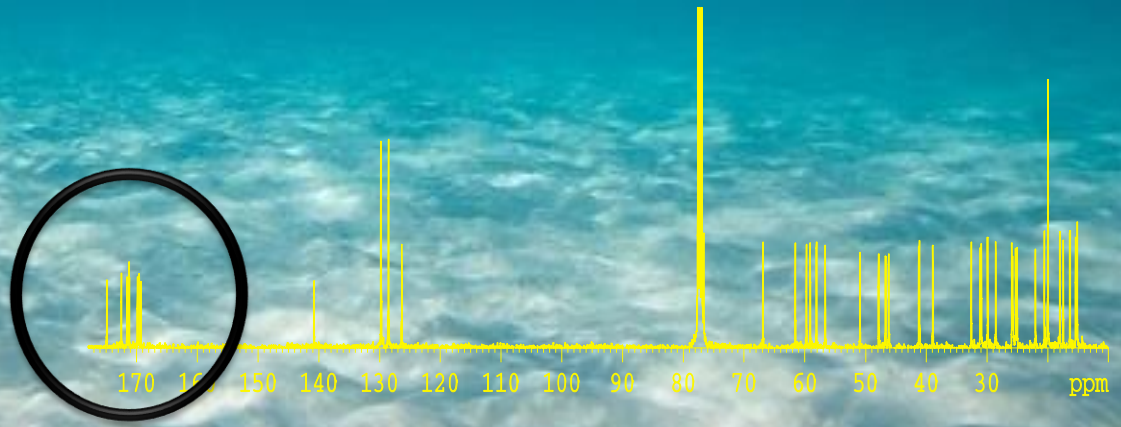
Polypeptides NMR

13C NMR spectrum

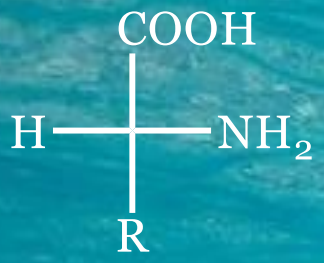
Ester/amide carbonyls (δ 168.0 to 175.0 ppm)





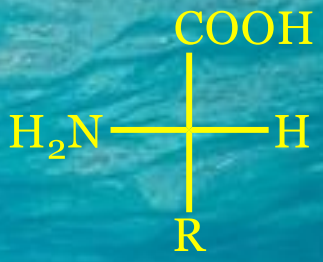


D-amino acids and L-amino acids in polypeptides



D-Amino Acid

D-amino acids and L-amino acids



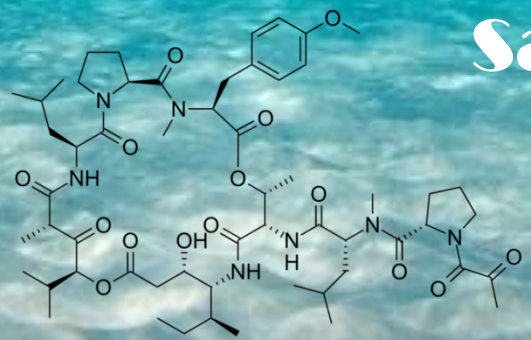
L-Amino Acid

D-amino acids

Toxic to Human

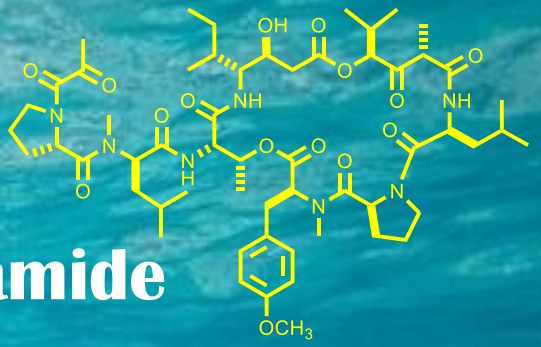
L-amino acids

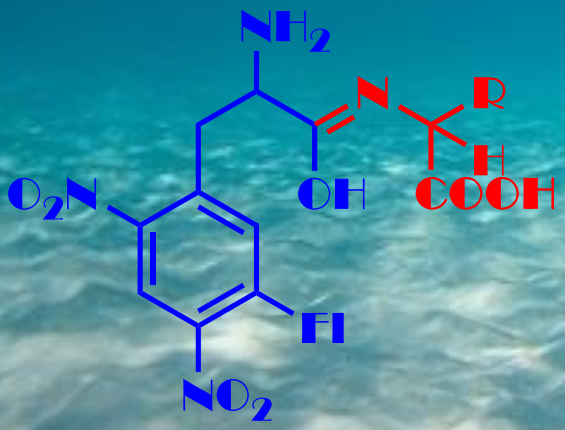
Safe to Human

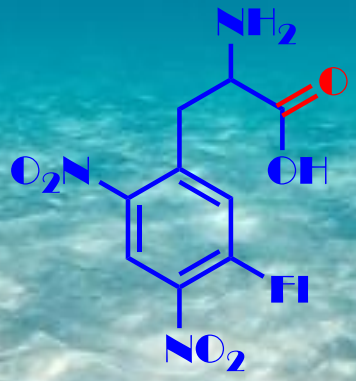


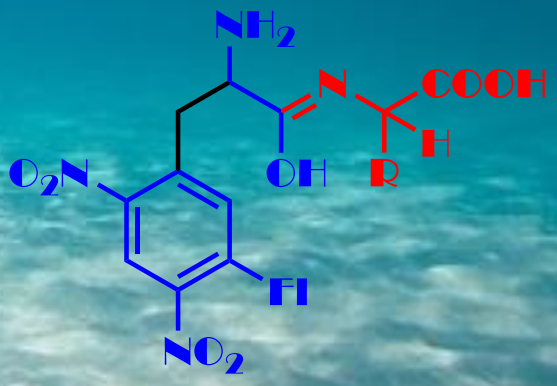
Marfey's Reagent

- Hydrolysis 20-200 ugm polypeptides
- 6 N HCl in a vial then reaction with
- 1-Fluoro, 2, 4 dinitro-5phenylalanine amide {**Marfey's reagent**}
- Chiral stationary phase HPLC
- Standard L-amino acids and D-amino acids reacted with Marfey's reagent as references.

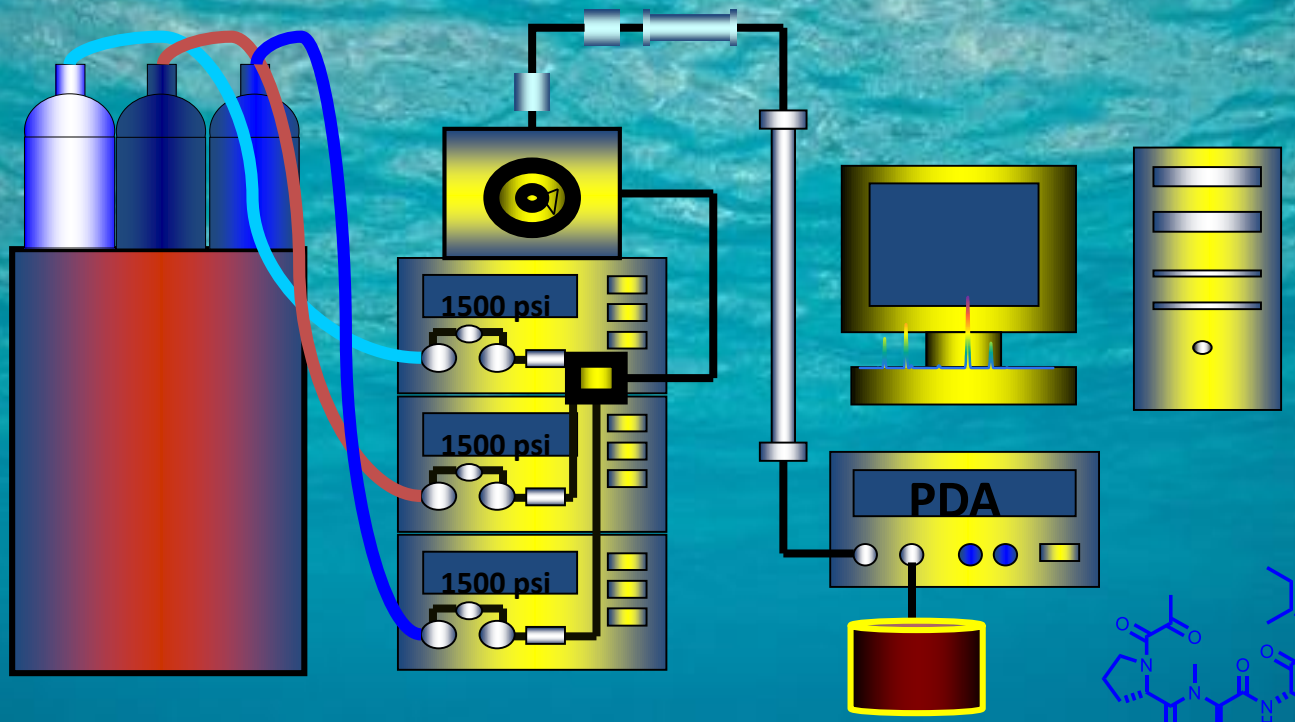


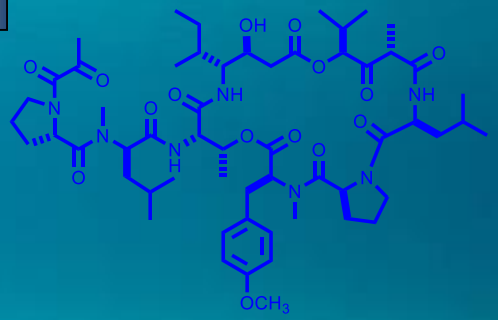






Marfey's Reagent





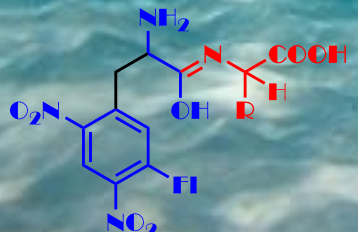
D-Isoleucine

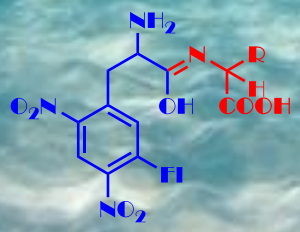
L-Glycine

D-Glycine

L-Isoleucine

Standards

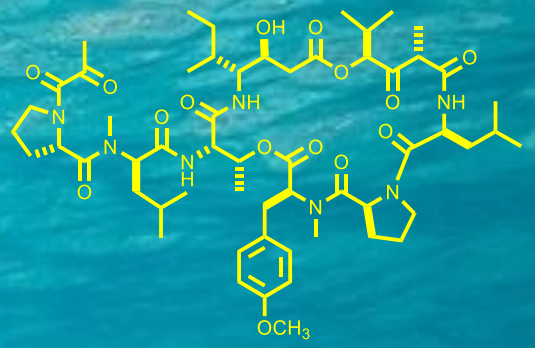


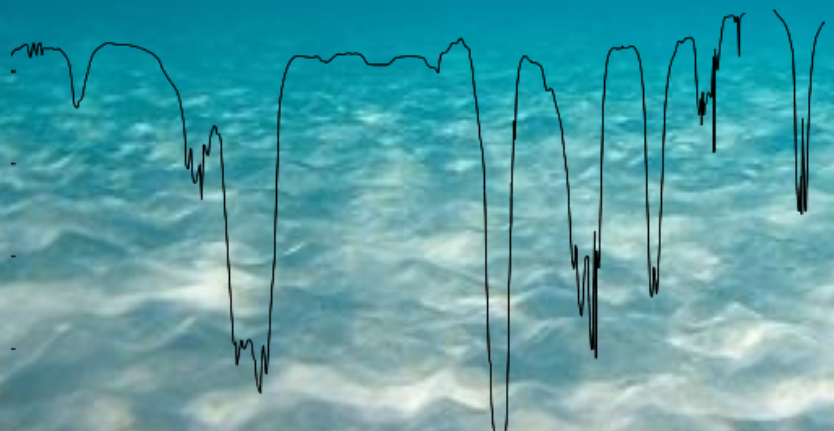


Sample

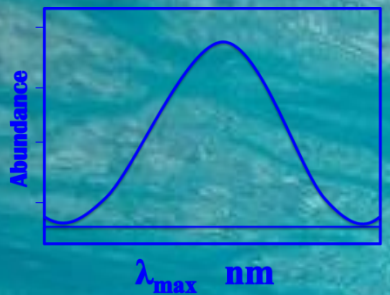
Depsipeptides

- Using pepsin enzyme
- Amide groups1650 cm^{-1}
- Ester group1730 cm^{-1}
- ^{1}HNMR: NH 6.40 – 6.95 ppm
  N-CH_3 2.85 – 3.10 ppm
- ^{13}CNMR gives us an idea about:
  - Amides and esters165-175 ppm

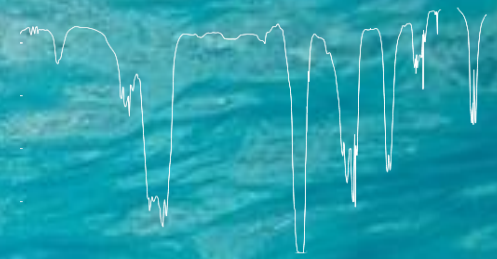




Aromatic Amino Acids in Polypeptides

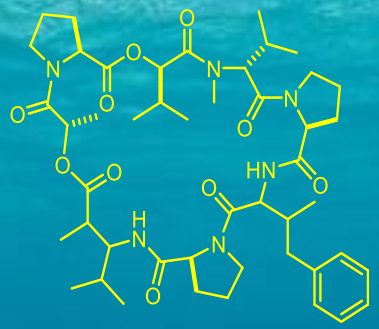


Aromatic Amino Acids



UV Sectroscopy

λmax 280 nm



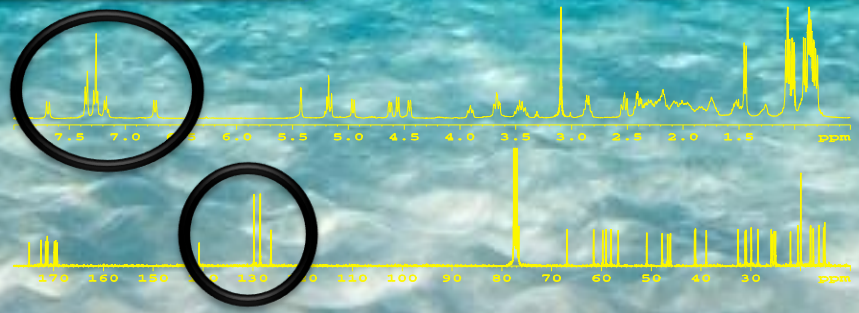
IR Spectroscopy

3000 - 3200 cm-1

^{1}HNMR Spectroscopy

6.8 – 8.2

ppm



^{13}CNMR Spectroscopy

110 – 150

ppm

Culturing of Marine Microorganisms

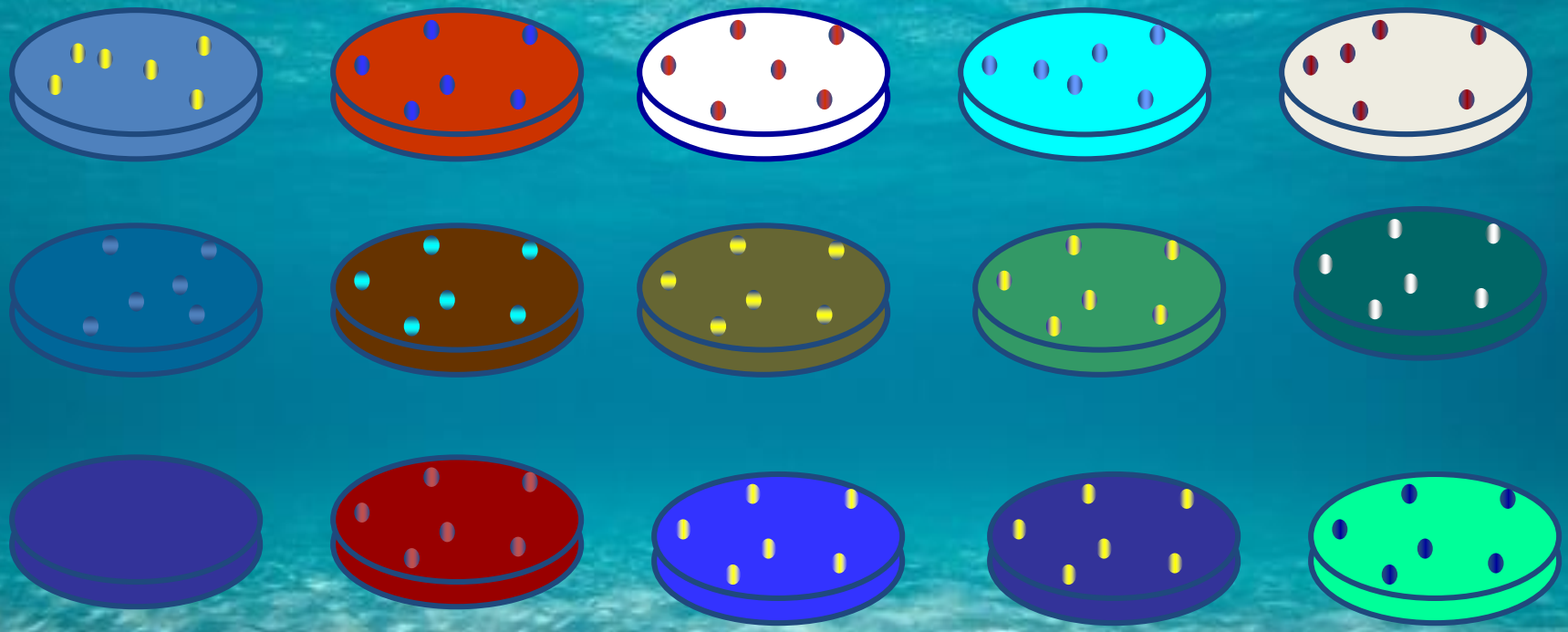
1 ml Sea water

About 0.1% of the

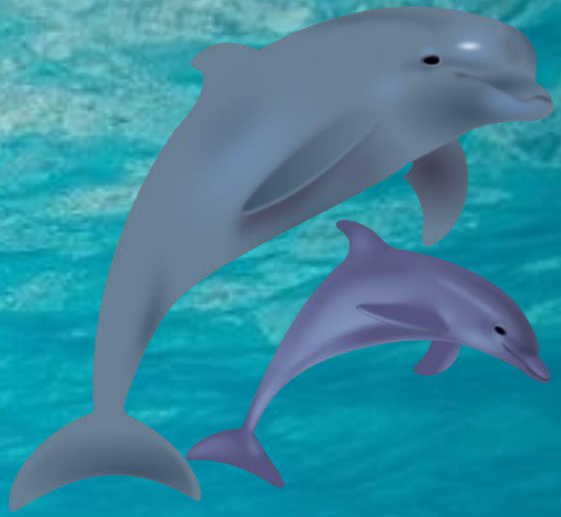
Microorganisms grown

HTPS {High Throuput Screening Technique}

HTPS High Throughput Screening



About 0.1% of the Microorganisms grown



Thank You